UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/820,679 | 04/08/2004 | Ian Hunter | 65689CPDV(43382) | 8534 |

21874 7590 11/07/2008

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

| EXAMINER | |
|---|---|
| SODERQUIST, ARLEN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1797 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 11/07/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/820,679 | HUNTER ET AL. | |
| | Examiner | Art Unit | |
| | Arlen Soderquist | 1797 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-26-08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 26,2008 has been entered.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1 and 3-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schellenberger (US 6,027,873) in view of Franzen (US 5,770,860) or Little (US 6,024,925, newly cited and applied) and de Macario (US 4,682,890). In the patent Schellenberger teaches a method for holding samples for analysis and an apparatus thereof includes a testing plate with a pair of opposing surfaces and a plurality of holes. Each of the holes extends from one of the opposing surfaces to the other one of the opposing surfaces. The holes are arranged in groups, where each group has at least two rows and two columns of holes. The groups are arranged in sets, where each set has at least two rows and two columns of groups. To analyze samples, at least one of the opposing surfaces of the testing plate is immersed in a solution to be analyzed. A portion of the solution enters openings for each of the holes in the immersed opposing surface. Once the holes are filled with solution, the testing plate is removed and is held above a supporting surface. Surface tension holds the solution in each of the holes. The solution in one or more of the holes is then analyzed and the solution in one of these holes is identified for

further study. The location of the identified solution is marked based upon its location within a particular set and group of holes. Columns 2-3 teach the formation of the plate and the variability in diameter and spacing depending on the needs and surface tension required to hold the liquid. The process does not necessarily place the same sample in each through-hole and some through holes may not contain anything to be analyzed. While the system is designed to be used without any pipetting apparatus, it does not teach that special pipetting apparatus cannot be used.

In the patent Franzen teaches a method for rapid loading of large sample supports with a very large number of analyte samples for mass spectrometric analysis using the ionization method of matrix-assisted desorption by laser bombardment (MALDI). The method consists of using microtiter plates already introduced in biochemistry and molecular genetics for parallel processing of a large number of dissolved samples and a multiple pipette unit for simultaneous transfer of sample solution quantities from all reaction wells on a microtiter plate to the sample support, the sample support having at least the same size. By repeated loading with samples from other microtiter plates, spaced between the samples already applied, a very high density of samples can be achieved. Some of these samples can be reserved for a mass spectrometric determination of the sample positioning on the sample support, and the positions of the other samples can then be interpolated. The basic idea is to adapt the sample support in its size and shape to microtiter plates and to transfer all (for example 384) or at least a large subset of analyte samples from one microtiter plate onto the MALDI layer at the same time. Suitable for this transfer is the well-known multiple pipette unit which either has exactly as many pipettes as the microtiter plates has reaction wells, or at least a large subarray of pipettes. The array of micropipettes must possess the same spot spacing as the reaction wells on the microtiter plate, or an integer multiple thereof. When using microtiter plates with 384 analysis samples, preferredly all 384 samples may be transferred at the same time and placed in a sample spot array with 4.5 millimeter spot spacing on the support. As an alternative, a multipipette with 96 pipette tips may be used, yielding a sample spot array with 9 millimeter spot spacing, but necessitating four sample transfers from one 384-well microtiter plate. By cleaning the multipipettes, changing the microtiter plates and repeating this procedure, a second sample spot array with another 384 analysis samples from a second microtiter plate can be applied to the same sample support, whereby this sample spot array is just slightly offset (interlaced) from the first array. By

repeating this procedure, 384 sample blocks (or, in the case of a 96-tip multipipette, 96 sample blocks) can be created on a sample support, while each sample point block contains a large number of sample spots each of which comes from a different microtiter plate. For example, with a block of 5 by 5 sample spots and using a 384-well microtiter plate and a 384-tip pipette, a total of 5 X 5 X 384 = 9,600 samples can be applied while the sample spots can be spaced at a maximum of 0.9 millimeters from one another. The sample spots can each have a diameter of about 0.6 millimeters without problem. It is even possible to apply blocks of 11 by 11 sample spots with 400 micrometers of spacing and 300 micrometers diameter for each sample spot. This produces a total load of 46,464 samples on a single sample support plate. As shown below, even many more analysis samples can be applied. The multiple pipette unit contains the pipettes exactly in the spacing of the array of reaction wells on the microtiter plate (or in integer multiples of the distances). The pipettes can therefore reach into the reaction containers with spatial precision and synchronicity and take out the solution there. They can, for example, terminate in small steel capillaries of 200 micrometers in outside diameter which are arranged in conically pointed holders with extreme precision in the grid of the microtiter plates of 4.5 millimeters. With them, very precise sample spots of 200 micrometers diameter are produced on the MALDI layer of the sample support which are arranged exactly in the grid of the microtiter plate. The amount of sample in those spots is by far sufficient for a single mass spectrometric analysis. The pipettes can be designed as a large number of individual microliter syringes with synchronous movement of the plungers.

In the little patent a system and method for preparing low volume analyte arrays is taught. The system includes serial and parallel dispensing tools that can deliver defined and controlled volumes of fluid to generate multi-element arrays of sample material on a substrate surface. The substrates surfaces can be flat or geometrically altered to include wells of receiving material. In one embodiment, the invention provides a tool that allows the parallel development of a sample array. To this end, the tool can be understood as an assembly of vesicle elements, or pins, wherein each of the pins can include a narrow interior chamber suitable for holding manual liter volumes of fluid. Each of the pins can fit inside a housing that forms an interior chamber. The interior chamber can be connected to a pressure source that will control the pressure within the interior chamber to regulate the flow of fluid within the interior chamber of the pins. Figures

5A-5D show one method for dispensing fluids. In this embodiment, the robotic assembly (16) employs a pin tool assembly (38) that is configured similarly as the pin tool assembly (50) depicted in figure 2. In a first step, (figure 5A), the program can direct the robotic assembly to move the pin assembly above the source plate (20). The robotic assembly will then dip the pin assembly into the source plate (e.g. a 384 well plate). As shown in figure 4 the pin assembly can include 16 different pins such that the pin assembly will dip 16 pins into different 16 wells of the 384 well DNA source plate. Next, the data processor (12) will direct the motion controller (14) to operate the robotic assembly to move the pin assembly to a position above the surface of the substrate (34). The substrate can be any substrate suitable for receiving a sample of material and can be formed of silicon, plastic, metal, or any other such suitable material. The program can then direct the robotic assembly, to eject fluid from into a respective well (92) of the substrate (90). The data processor can run a computer program that controls and regulates the volume of fluid dispensed. The program can direct the controller to eject a defined volume of fluid, either by generating a spray or by forming a drop that sits at the end of the vesicle, and can be contacted with the substrate surface for dispensing the fluid thereto. Figures 5C and 5D show the earlier steps shown in figures 5A-5B can again be performed, this time at a position on the substrate surface that is offset from the earlier position. In the depicted process, the pin tool is offset by a distance equal to the distance between two wells.

In the patent de Macario describes a carrier and a microsample holder (30) for use in horizontal beam spectrophotometers in place of conventional cuvette supports that normally are used with such spectrophotometers. The microsample holder is formed as a plate having a number of retaining elements preferably in the form of a circular perforated areas for retaining drops of samples to be analyzed by the spectrophotometer. Columns 2-3 teach a sample holder of similar design is known for vertical beam spectrometers. Columns 7-8 teach that the holder (30) is formed with a set of retaining elements, such as a row of four retaining elements (32,34,36,38). The retaining elements are of circular shape having diameters on the order of about 3 mm, each retaining element being capable of retaining a 5-10 μ1 sample of liquid to be analyzed. The surfaces of holder (30) other than the circular areas may be coated with a thin layer of hydrophobic material to assure retention of the liquid samples within the circular areas. The circular hole diameter permits the surface tension of the liquid sample to retain that sample

stably within the confines of the hole. The remainder of holder (30) need not be light transmissive, it is, nevertheless, advantageous to its construction to construct the plate of transparent material, such as glass, plastic, quartz or the like. The holder (30) may be modified within the scope of the invention to have two or more rows of retaining elements, if desired, such as the rectangular pattern shown in figure 5 and described in column 7, lines 45-61 or column 11, lines 6-28. It is recognized that the holder is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers to pass through the center of each sample retained by retaining elements. In this respect the paragraph bridging columns 7-8 teaches that since the overall height, length and width of the carrier are identical (or substantially identical) to the height, length and width of the conventional cuvette support, the carrier is readily usable with the normal support-receptacle and automatic or manual indexing mechanism of conventional horizontal beam spectrophotometers. Thus, the retaining elements are aligned with the analyzing beam that normally passes through windows of the conventional cuvette support. It is seen that the analyzing beam thus passes through the center of each sample retained by retaining elements. The beam passes through only one sample at a time, and as the carrier is indexed, and successive samples are exposed to the beam. The patent also teaches that the de Macario device is meant to reduce the amount of sample required for the testing. The paragraph bridging columns 10-11 teaches the addition of reagents and samples to the holes of the device. In particular figure 8 and its associated description in column 10 teach registration of a plurality of carriers with a nonzero distance between them such that when fluid is added to one of the retaining elements a liquid bridge is formed between retaining elements on adjacent plates.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a method as taught by Franzen or Little for depositing a number of different fluids in each of the through-hole of Schellenberger to increase the speed as taught by Franzen because of the ability to produce through holes each having a different sample or reagent therein as taught by de Marcario rather than the random possibility of producing through-holes with measurable sample therein. It would have been obvious to one of ordinary skill in the art at the time the invention was made to place a plurality of the Schellenberger plates adjacent to each other as taught by de Macario because it would allow the fluid to be placed into more than one

plate at a time as taught by de Macario through the liquid bridge taught by de Macario. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to use any of the pipet, capillary and syringe types of transfer devices described by Franzen to transfer solutions to the Schellenberger plate because of their utility to be used in that manner as shown by Franzen and de Macario.

4. Applicant's arguments filed August 26, 2008 have been fully considered but they are not persuasive. Examiner does not agree with applicant regarding the obviousness of the claims. Relative to the stacked array, the de Macario reference, in figure 8 and its associated description, teach a plurality of arrays that are placed adjacent to each other by a small non-zero distance that allows a liquid bridge to form allowing fluid to be transferred to retaining elements that are adjacent to one another. Relative to the Schellenberger reference, it is clear that the prior art of Schellenberger included pippeting devices. Their disadvantage as taught by Schellenberger was that they are expensive. However if one of skill in the art were not concerned with the cost of the dispensing apparatus, the Franzen or Little type of dispensing would have been obvious because of the ability to load multiple solutions at the same time. The de Macario reference is clear that it is surface tension that holds the liquid in the holes. Additionally, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this instance the Franzen and Little references clearly show that liquid can be aspirated from a device such as wells of a microtiter plate and deposited at locations that are spaced at a fraction of the well to well spacing in the microtiter plate. It should also be noted that the spacing between the holes and the size of the holes has not been defined other to say that the spacing is a fraction of the well to well spacing of the microtiter plate. Thus the spacing of the instant claims includes a spacing that is one half the microtiter spacing. The Franzen and Little references clearly show that level of positioning accuracy. Figure 2 of Franzen shows a level of positioning accuracy that is at least good enough to add liquid to the holes of figure 1 of Schellenberger. (Column 3, lines19-29, teach spacings as small as 400 micrometers.)

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited prior art are directed to pipetting devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (571)272-1265. The examiner can normally be reached on Monday-Thursday and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Arlen Soderquist/
Primary Examiner, Art Unit 1797